

APPLN. FILING DATE: JULY 9, 2001

TITLE: HUMAN BASIC FIBROBLAST GROWTH FACTOR ANALOG

INVENTOR(S): JOHN C. FIDDLER, ET AL.

APPLICATION SERIAL NO: 09/902,460

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FIG. 1-1

Human Basic Fibroblast Growth Factor

10 20 30 40 50 60 70
AATTCACTGCC TCTTCTCTC CTTTGTGG TAGACGACTT CAGCCTCTGT CCTTTAATT TAAAGTTAT

80 90 100 110 120 130 140
GCCCACTTG TACCCCTCGT CTTTGGTGA TTTAGAGATT TTCAAAGCCT GCTCTGACAC AGACTCTTCC

150 160 170 180 190 200 210
TTGGATTGCA ACTTCTCTAC TTTGGGTGG AACCGGCTTC TCCGTTTGA AACGCTAGCG GGGAAAAAAT

220 230 240 250 260 270 280
GGGGGAGAAA GTTGAGTTA AACTTTAAA AGTTGAGTCA CGGCTGGTTG CGCACGAAA GCCCCGCAGT

290 300 310 320 330 340 350
GTGGAGAAAG CCTAACGTG GTTTGGTGG TGCGGGGTT GGGCGGGGT GACTTTGGG GGATAAGGGG

360 370 380 390 400 410 420
CCGTGGAGCC CAGGAATGC CAAAGCCCTG CCGCGGCCCTC CGACGCGCGC CCCCCGCCCTC TCGCCTCTCC

430 440 450 460 470 480 490
CCCGCCCCCG ACTGAGGCCG GCCTCCCCCG CGGACTGATG TCGCGCGCTT CGGTGTTGTG GCCGAAGCCG

500 510 520 530 540 550 560
CCGAACTCAG AGGCCGGCCC CAGAAAACCC GAGCGAGTAG GGGCGGGCGC GCAGGAGGGA GGAGAACTGG

570 580 590 600 610 620 630
GGGCGGGGA GGCTGGTGGG TGTGGGGGT GGAGATGTAG AAGATGTGAC GCCGCGGCCCG GGCGGGTGGCC

640 650 660 670 680 690 700
AGATTAGCGG ACGGCTGCC CCGGTTGCAA CGGGATCCCC GGCGCTGCAG CTTGGGAGGC GGCTCTCCCC

710 720 730 740 750 760 770
AGGCGCGTC CGCGGAGACA CCCATCTGTG AACCCCAGGT CCCGGGCCGC CGGCTCGCCG CGCACCAAGGG

780 790 800 810 820 830 840
GCCGGCGGAC AGAAGAGCGG CCGAGCGGCT CGAGGCTGGG GGACCGCGGG CGCGGCCGG CGCTGCCGGG

850 860 870 880 890 900 910
CGGGAGGCTG GGGGGCCGGG CCCGGGGCG TGCCCGGAGC GGCTCGGAGG CGGGGGCCGG GGCGGGGGGA

920 930 940 950 960
CGCCGGCTCC CGCGCGGGCT CCAGCGGCTC GGGGATCCCC GCCGGGCCGC GCAGGGACC ATG GCA GCC
Met Ala Ala

984 999 1014 1029
GGG AGC ATC ACC ACG CTG CCC GCC TTG CCC GAG GAT GCC GGC AGC GGC CCC TTC CGC
Gly Ser Ile Thr Thr Leu Pro Ala Leu Pro Glu Asp Gly Gly Ser Gly Ala Phe Pro

1044 1059 1074 1089
CCC GGC CAC TTC AAG GAC CCC AAG CGG CTG TAC TGC AAA AAC GGG GGC TTC TTC CTG
Pro Gly His Phe Lys Asp Pro Lys Arg Leu Tyr Cys Lys Asn Gly Gly Phe Phe Leu

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FIG. 1-2

1104 1119 1134 1149
CGC ATC CAC CCC GAC GGC CGA GTT GAC GGG GTC CGG GAG AAG AGC GAC CCT CAC ATC
Arg Ile His Pro Asp Gly Arg Val Asp Gly Val Arg Glu Lys Ser Asp Pro His Ile

1164 1179 1194
AAG CTA CAA CTT CAA GCA GAA GAG AGA GGA GTT GTG TCT ATC AAA GGA GTG TGT GCT
Lys Leu Gln Leu Gln Ala Glu Glu Arg Gly Val Val Ser Ile Lys Gly Val Cys Ala

1224 1239 1254
AAC CGT TAC CTG GCT ATG AAG GAA GAT GGA AGA TTA CTG GCT TCT AAA TGT GTT ACG
Asn Arg Tyr Leu Ala Met Lys Glu Asp Gly Arg Leu Leu Ala Ser Lys Cys Val Thr

1269 1284 1299 1314
GAT GAG TGT TTC TTT GAA CGA TTG GAA TCT AAT AAC TAC AAT ACT TAC CCG TCA
Asp Glu Cys Phe Phe Glu Arg Leu Glu Ser Asn Asn Tyr Asn Thr Tyr Arg Ser

1329 1344 1359 1374
AGG AAA TAC ACC AGT TGG TAT GTG GCA TTG AAA CGA ACT GGG CAG TAT AAA CTT CGA
Arg Lys Tyr Thr Ser Trp Tyr Val Ala Leu Lys Arg Thr Gly Gln Tyr Lys Leu Gly

1389 1404 1419 1434
TCC AAA ACA GGA CCT GGG CAG AAA GCT ATA CTT TTT CTT CCA ATG TCT GCT AAG AGC
Ser Lys Thr Gly Pro Gly Gln Lys Ala Ile Leu Phe Leu Pro Met Ser Ala Lys Ser

1450 1460 1470 1480 1490 1500
TGA TTT TAATGGCCAC ATCTAATCTC ATTTCACATG AAAGAAGAAG TATATTTAG AAATTTGTTA

1510 1520 1530 1540 1550 1560 1570
ATGAGAGTAA AAGAAAATAA ATGTGTATAG CTCAGTTGG ATAATTGGTC AAACAATTT TTATCCAGTA

1580 1590 1600 1610 1620 1630 1640
GTAAAAATATG TAACCATGCC CAGTAAAGAA AAATAACAAA AGTTGTAAAA TGTATATTCT CCCTTTATA

1650 1660 1670 1680 1690 1700 1710
TTGCATCTGC TGTTACCCAG TGAAGCTTAC CTAGACCAAT GATCTTTTC ACGCATTGTC TTTATTCGAA

1720 1730 1740 1750 1760 1770 1780
AAGAGGCTTT TAAAATGTGC ATGTTTAGAA AACAAAATTG CTTCATGGAA ATCATATACA TTAGAAAATC

1790 1800 1810 1820 1830 1840 1850
ACAGTCAGAT GTTTAATCAA TCCAAAATG TCCACTATTG CTTATGTCAT TCGTTAGTCT ACATGTTCT

1860 1870 1880 1890 1900 1910 1920
AAACATATAAA ATGTGAATTT AATCAATTCC TTTCATAGTT TTATAATTCT CTGGCAGTTC CTTATGATAG

1930 1940 1950 1960 1969
AGTTTATAAA ACAGTCCTGT GTAAACTGCT CGAACGTTCTT CCGGAATTC

FIG. 2

Human Acidic FGF

27 54
TGC ATT TTG TGC CTT TGC TGG AAG AAC CGA CTA CAG GTT TGT TCA ATT TCT TAC
81 108
AGT CTT GAA AGC GCC ACA AGC AGC TGC TGA GCC ATG GCT GAA GGG GAA ATC
MET Ala Glu Gly Glu Ile
1
135 162
ACC ACC TTC ACA GCC CTG ACC GAG AAG TTT AAT CTG CCT CCA GGG AAT TAC AAG
Thr Thr Phe Thr Ala Leu Thr Glu Lys Phe Asn Leu Pro Pro Gly Asn Tyr Lys
10 20
189 216
AAG CCC AAA CTC CTC TAC TGT AGC AAC GGG GGC CAC TTC CTG AGG ATC CTT CCG
Lys Pro Lys Leu Leu Tyr Cys Ser Asn Gly Gly His Phe Leu Arg Ile Leu Pro
30 40
243 270
GAT GGC ACA GTG GAT GGG ACA AGG GAC AGG AGC GAC CAG CAC ATT CAG CTG CAG
Asp Gly Thr Val Asp Gly Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln
50 60
297 324
CTC AGT GCG GAA AGC GTG GGG GAG GTG TAT ATA AAG AGT ACC GAG ACT GGC CAG
Leu Ser Ala Glu Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln
70
351 378
TAC TTG GCC ATG GAC ACC GAC GGG CTT TTA TAC GGC TCA CAG ACA CCA AAT GAG
Tyr Leu Ala MET Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu
80 90
405 432
GAA TGT TTG TTC CTG GAA AGG CTG GAG GAG AAC CAT TAC AAC ACC TAT ATA TCC
Glu Cys Leu Phe Leu Glu Arg Leu Glu Asn His Tyr Asn Thr Tyr Ile Ser
100 110
459 486
AAG AAG CAT GCA GAG AAG AAT TCG TTT GTC GGC CTC AAG AAG AAT CCC ACC TCC
Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys Asn Gly Ser Cys
120 130
513 540
AAA CGC CGT CCT CGG ACT CAC TAT GGC CAG AAA GCA ATC TTG TTT CTC CCC CTG
Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala Ile Leu Phe Leu Pro Leu
140 150
567 594
CCA GTC TCT TCT GAT TAA AGA GAT CTG TTC TGG GTG TTG ACC ACT CCA GAG AAG
Pro Val Ser Ser Asp
155
621
TTT CGA CGG GTC CTC ACC TGG TTG ACC CAA AAA TGT TCC CTT GA

Comparison of amino acid sequence of
human basic and acidic FGF
(basic/acidic)

		Heparin binding domain		Receptor binding domain	
1	10	20	30	40	50
MAAGSITTPALPEDGGSGAFPPGHPDKR	LYCKNGGFFLRIHPDGRV	VREKSDPHI			60
MAEGEITTFALTEKFNL	KKPKULLYCSNGGHFLRI	LPDGTV	DGT	DRSDQH	I
1	10	20	30	40	50
KLQLQAEERGVVSIKGVCANRYLAM	KEDG	LLASKC	VTC	DECFF	FERNN
QLQLSAESVGEVYIKSTETGQYLAM	DTDGLLYGSQ	TPN	YRSRKY		120
60	70	80	90	100	110
TS--wYVALKRTGQYKLGS	GTGPKAILFLPMSAKS				
AEKNWFVGLUKKNGSCKRGPR	THYGGQKAILFLPLPVSSD	Receptor binding domain			Heparin binding domain
120	130	140	150		

FIG. 3

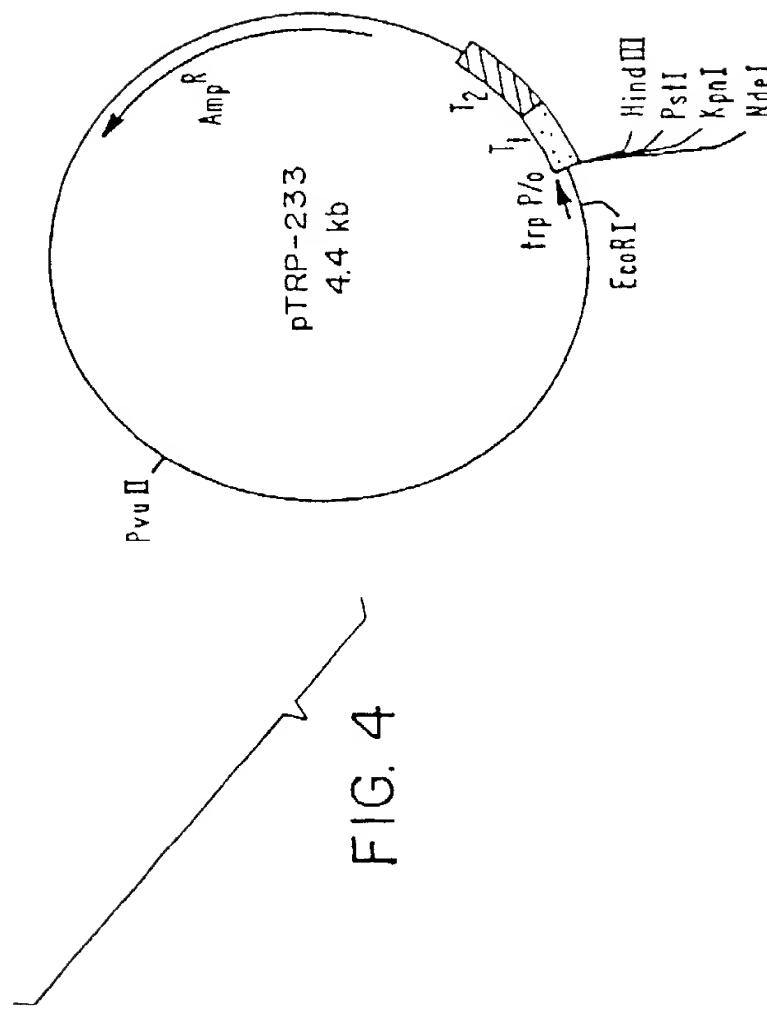
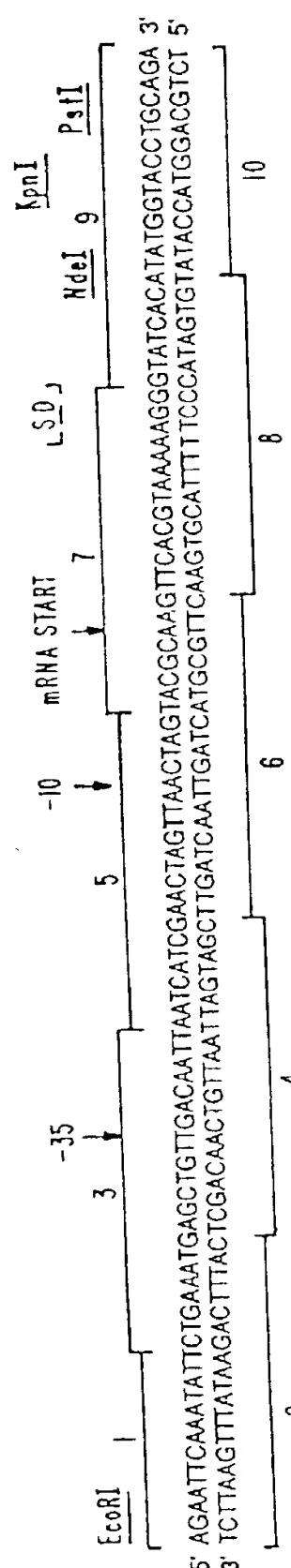


FIG. 4

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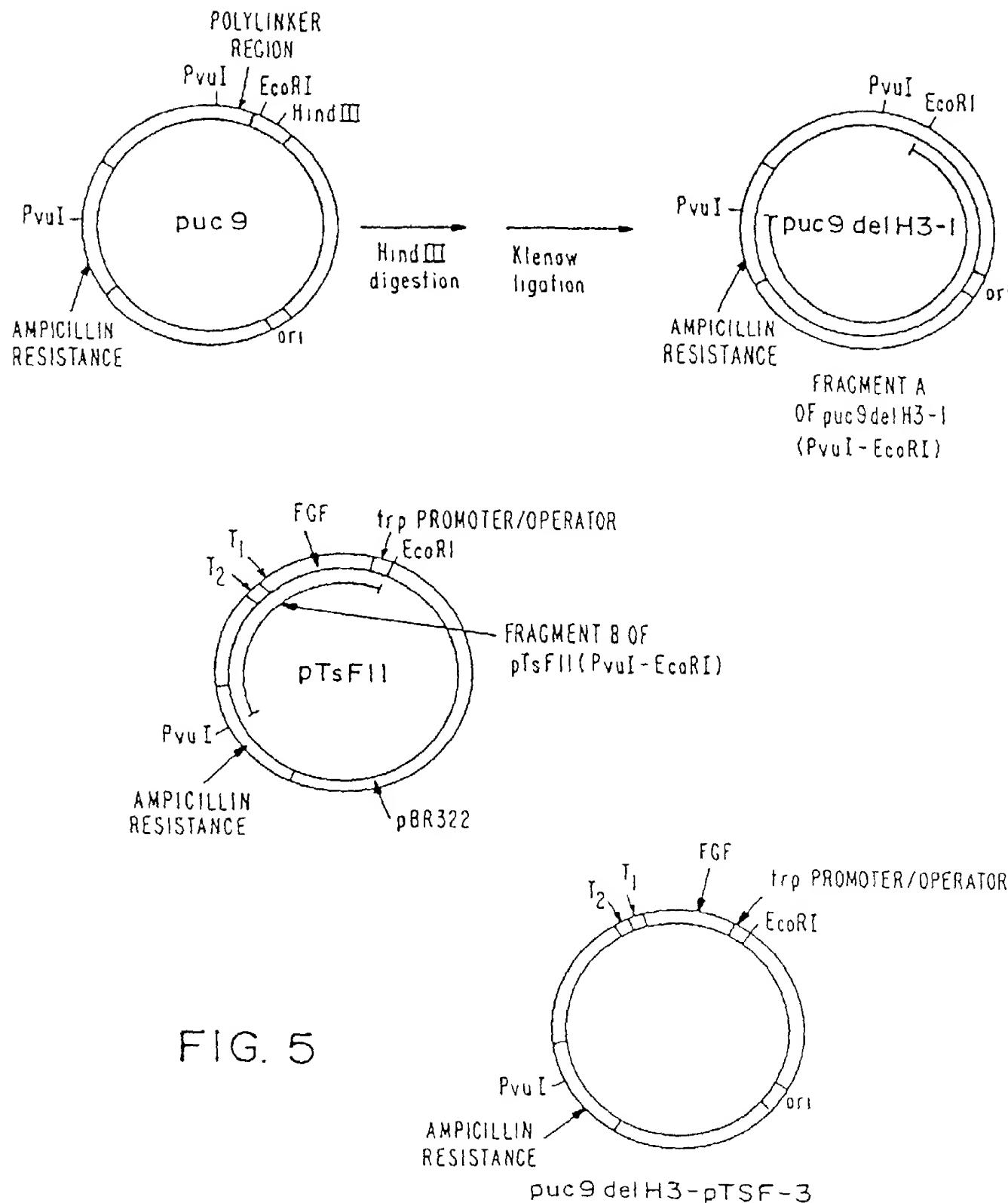


FIG. 5

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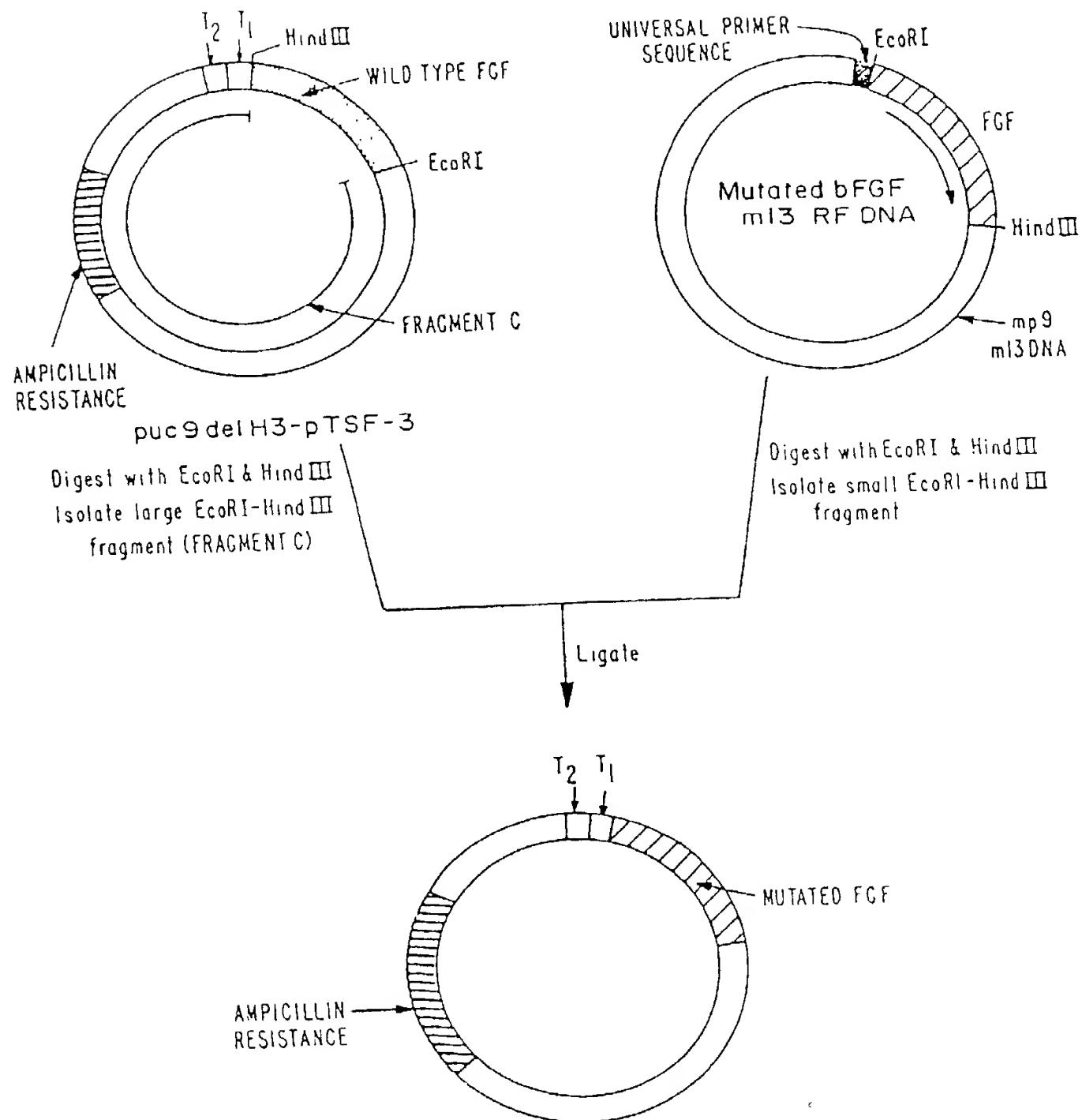


FIG. 6

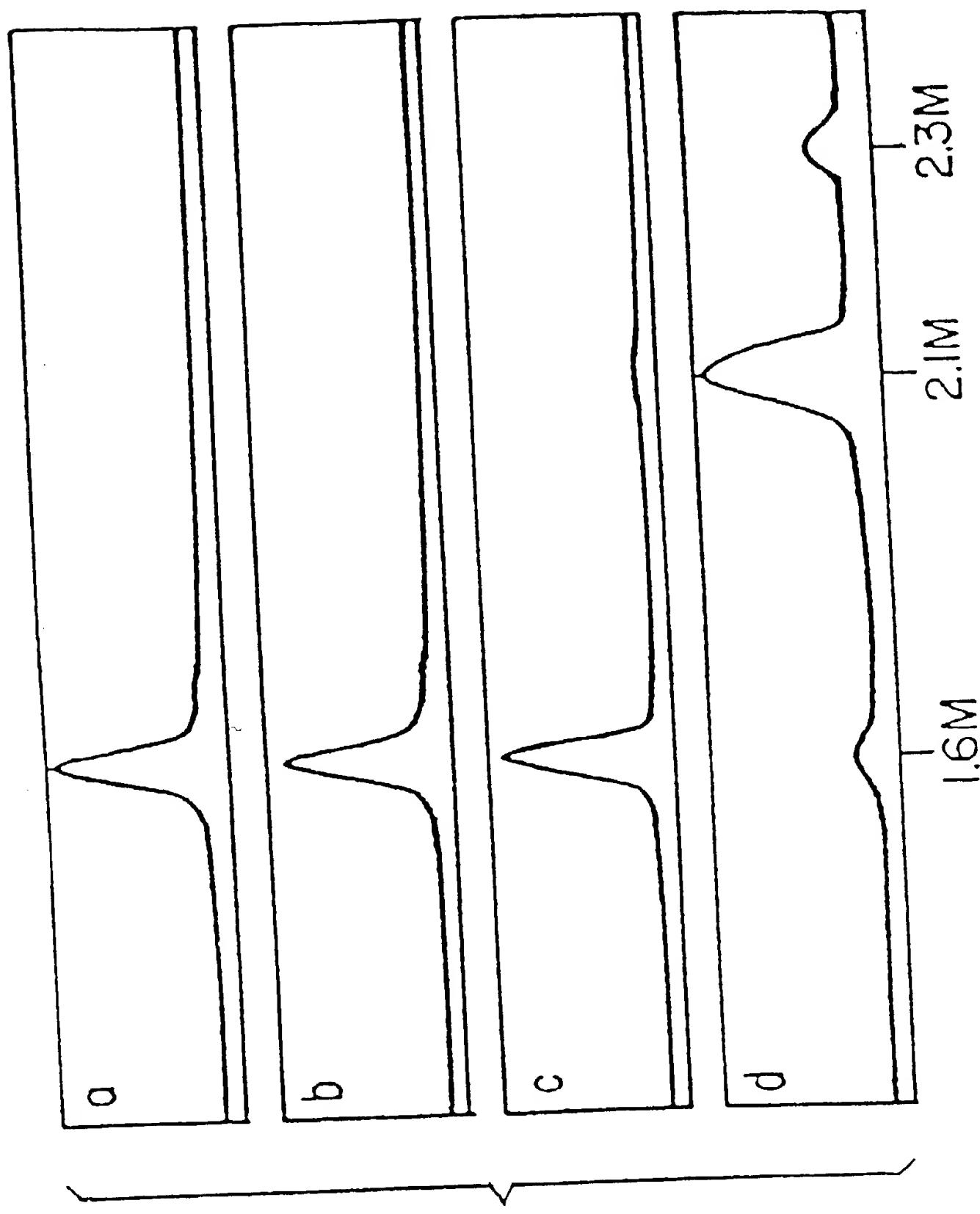


FIG. 7